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EPPS, JANET L

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20

Application Number: 09/374,704
Filing Date: August 12, 1999
Appellant(s): BAIRD ET AL.

Michael A. Whittaker
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 10-15-2001.

(1) *Real Party in Interest*

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A statement identifying the real party in interest is contained in the brief.

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

The rejection of claims 1, 3-19 and 25-26 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7). Claims 1, 3-19 and 25-26 are all rejected under the same grounds and should therefore stand or fall together for this reason.

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

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- ⌘ Feng et al. "Hin Recombinase Bound to DNA: The Origin of Specificity in Major and Minor Groove Interactions." *Science*, Vol. 263 (January 21, 1994), pp. 348-355.
- Parks et al. "Recognition of 5'-(A,T)GG(A,T)2-3' Sequences in the Minor Groove of DNA by Hairpin Polyamides." *Journal of the American Chemical Society*, Vol. 118 (1996), pages 6153-6159.
- ⌘ Swalley et al. Recognition of a 5'-(A,T)GGG(A,T)2-3' Sequence in the Minor Groove of DNA by an Eight-Ring Hairpin Polyamide. *Journal of the American Chemical Society*, Vol. 118 (1996), pages 8198-8206.
- ⌘ Trauger et al. "Extension of Sequence-Specific Recognition in the Minor Groove of DNA by Pyrrole-Imidazole Polyamides to 9-13 Base Pairs." *Journal of the American Chemical Society*, Vol. 118 (1996), pages 6160-6166.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 3-19 and 25-26 stand finally rejected under 35 U.S.C. 103(a) as being unpatentable over Swalley et al., Parks et al. and Trauger et al. in view of Feng et al.

Claims 2-3 read on the polyamides of claim 1 further comprising a first and second amino acid, wherein said first amino acid is selected from arginine, proline, lysine, and hydroxyproline, and said second amino acid is selected from proline, glycine, serine, threonine, leucine, isoleucine, valine, alanine, and hydroxyproline.

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Claims 6-7 read on a polyamide of claim 1 wherein said positively charged groups is arginine, lysine, or histidine, claim 8 recites wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

Swalley et al. (Figure 2, structure 2, page 8200), Parks et al. (Figure 2, page 6154) or Trauger et al. (Figure 3, page 6162) disclose polyamides comprising N-methylimidazole and N-methylpyrrole, and N,N-dimethylaminopropylamide moieties, and one or more non-alpha amino acids such as γ -aminobutyric acid or β -alanine, and further bearing a terminal positively charged group. Additionally each reference disclose polyamides bearing hairpin linkages derived from γ -aminobutyric acid. The polyamides disclosed in each of these references were specifically designed to provide specific recognition of DNA sequences located in the minor groove of DNA molecules (see the abstract of each reference).

However, the cited references do not teach polyamides wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

Feng et al. disclose a polyamide compound which specifically interacts with the minor groove of DNA utilizing the sequence Gly₁₃₉-Arg₁₄₀-Pro₁₄₁-Arg₁₄₂ at the amino terminal domain, and binds to the major groove involving a helix-turn-helix α -helix motif. The binding of the polyamide to DNA results in a site-specific inversion reaction at the site of binding. This specific inversion reaction can be used to activate or inactivate gene expression (page 348, paragraphs 1-3).

Swalley et al., Parks et al. and Trauger et al. disclose polyamide compounds comprising one or more amino acids selected from N-methylpyrrole, and N-methylimidazole, wherein one or more of said amino acids are not α -amino acids for the reasons given above. It would have been

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obvious to one of ordinary skill in the art at the time of filing to modify these polyamides with a sequence comprising Arg-Pro-Arg, since polyamide compounds comprising these sequence were known to bind DNA with high affinity in a sequence specific manner. Thus providing additional polyamide compounds for DNA recognition. The ability to enlarge the sequence repertoire of a polyamide would have provided for "a universal approach for the recognition of any desired DNA sequence by strictly chemical methods (Swalley et al., p. 8200, para. 5)."

Therefore, the invention as a whole is *prima facie* obvious over Swalley et al., Parks et al. and Trauger et al. in view of Feng et al.

(11) Response to Argument

Appellants traverse the instant rejection on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness. Specifically, Appellants provided the following arguments: (1) The skilled artisan would lack motivation to select the three amino acid "Arg-Pro-Arg" sequence from the larger Hin recombinase molecule and combine this sequence with the polyamides of the Swalley, Parks and Trauger publications, because Arg and Pro are neither chemically nor functionally similar to the pyrrole-imidazole-based residues disclosed in the Swalley, Parks, and Trauger publications. (2) The skilled artisan would not have had motivation or reasonable expectation of success in combining the three amino acid "Arg-Pro-Arg" sequence with the polyamides of the Swalley, Parks, and Trauger publications to provide the instantly claimed polyamides, because these residues in isolation do not possess DNA binding characteristics. (3) The Examiner has inappropriately applied hindsight reconstruction of the claimed invention. (4) The Examiner did not specifically address the rationale with regard as to how the prior art references address claims 25-26.

(1-2) In contrast to Appellants arguments that there is no motivation to select the three amino acid sequence “Arg-Pro-Arg” from the Hin protein and combine them with the polyamides of the Swalley, Parks and Trauger publications, the Feng et al. reference clearly states that the “Arg-Pro-Arg” sequence maintains its ability to interact with the minor groove of DNA in a specific manner when positioned in an entirely different protein sequence, namely the Engrailed protein of *Drosophila* (page 355, 2nd paragraph). Moreover, Appellants argue that a person of ordinary skill in the art “would understand that it is only in the context of the entire Hin-recombinase 3-dimensional structure that the sequence would have any role in ‘[binding] DNA with a high affinity in a sequence specific manner,’” because an enormous number of other proteins also include the Arg-Pro-Arg sequence. However, Appellants did not provide any information with regards to the position of the Arg-Pro-Arg sequence within the numerous proteins listed in Appellant’s search. For example, there is no indication that the Arg-Pro-Arg sequence is positioned in the amino terminus of the proteins listed in Appellant’s search. In both the Hin recombinase and the Engrailed protein, the Arg-Pro-Arg sequence is positioned in the amino terminus, and it is in this environment that minor groove specific binding of DNA occurs by means of the Arg-Pro-Arg sequence (page 355, 2nd full paragraph). Based upon the position of the Arg-Pro-Arg sequence with in the Hin and Engrailed proteins amino terminus, one of ordinary skill in the art would have had a reasonable expectation of success for designing a functional minor groove specific DNA binding polyamide comprising an Arg-Pro-Arg sequence at the amino terminus of said polyamide. Therefore, there is clear expectation of success and motivation that suggest that the Arg-Pro-Arg sequence would maintain specific minor groove binding especially when positioned at a terminus of the molecule as the prior art has taught.

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In regards to Appellant's argument that Arg and Pro are neither chemically or functionally similar to the pyrrole-imidazole-based residues disclosed in the Swalley, Parks and Trauger publications, the examiner agrees that the pyrrole-imidazole compounds of these references are "structurally" different from the Arg-Pro-Arg residues disclosed in these references. However, contrary to Appellant's arguments, the arginine and proline residues are disclosed in Feng et al. as being functionally similar to the polyamide structures of Swalley, Parks and Trauger to the extent that the prior art discloses two examples wherein structures *comprising* the "Arg-Pro-Arg" sequence have demonstrated minor groove specific DNA binding. In like manner the polyamides of Parks et al., Swalley et al. and Trauger et al. comprising a combination of N-methylpyrrole, N,N dimethylamino-propylamide, and N-methylimidazole residues, exhibit minor groove specific DNA binding. Therefore, one of ordinary skill in the art would have recognized that the polyamides of Swalley, Parks, Trauger, and Feng et al. are capable of being used for the same purpose, specifically for binding sequences located within the minor groove of DNA molecules.

Furthermore, Feng et al. teaches that the ϵ -amine of the Arg side chain is capable of interacting with the N-3 group of Adenine, and the main chain amide of Arg permits a second hydrogen bond with the O-2 of Thymine (Feng et al. page 351, 3rd paragraph). Therefore, the structure of the Arginine molecule permits a stable interaction with A,T base pairs. Similarly, side by side pyrrole-pyrrole pairing in the polyamides of Parks et al., Swalley et al. and Trauger et al., permits binding to both A,T and T,A base pairs (Trauger et al., page 6160, 1st paragraph). This observation provides additional evidence that the polyamides of Parks et al., Swalley et al.

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and Trauger et al. are functionally similar to the Arg-Pro-Arg containing compounds of Feng et al.

It is also noted that the courts have previously decided that “[I]t is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted), see MPEP § 2144.06. In the instant case, the prior art has provided two examples wherein the sequence “Arg-Pro-Arg” is instrumental in providing minor groove specific binding to DNA, additionally the prior art clearly provide teaching wherein Pyrrole-Imidazole polyamides provide specific recognition of the minor groove of DNA. Therefore, it would have been *prima facie* obvious to form a combination of pyrrole-imidazole polyamides and the “Arg-Pro-Arg” amino acid in the formation of a third composition to be used for the purpose of minor groove specific binding of a DNA molecule.

Appellants also traverse the instant rejection on the grounds that “there is nothing of record in the asserted *prima facie* case to indicate that the skilled artisan would be motivated to select an Arg-Pro-Arg sequence, as disclosed in the Feng et al. publication, in order to disrupt interactions between proteins and the phosphate backbone or major groove of the DNA molecule.” Contrary to Appellant's arguments, the fact that Appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Furthermore, it is noted that the

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features upon which Appellant relies, namely that the Arg-Pro-Arg sequence is grafted to the polyamides in order to disrupt interactions between proteins and the phosphate backbone or major groove of the DNA molecule, are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(3) In response to Appellants traversal on the grounds that the Examiner has inappropriately applied hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Appellant's disclosure, such a reconstruction is proper. Such motivation was provided when the rejection was initially set forth and therefore provides for the proper reasoning to combine the prior art references. [MPEP § 2145.X.A]


(4) Appellants traverse the rejection of claims 25-26 on the grounds that the examiner did not specifically address the rationale with regard as to how the prior art references address claims 25-26, which relates to inhibiting gene expression using the claimed polyamides. First, it is interesting to note that Appellants never raised this issue until the filing of their appeal brief. Second Appellants should note that page 5, of the Office Action mailed 3-28-01, states in regards to the polyamide disclosed in Feng et al. "The binding of the polyamide to DNA results in a site-specific inversion reaction at the site of binding. This specific inversion can be used to activate or inactivate gene expression." Therefore, the examiner has addressed the relationship of the cited references with regards to "inhibiting gene expression using the claimed polyamides."

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Third, Appellant's own specification clearly states that polyamides, particularly those comprising N-methylpyrrole, and N-methylimidazole amino acids, are known in the art to "inhibit transcription factor binding and expression of a designated gene," and "offer a potentially general approach for gene regulation.." (page 2, lines 10-14) Thus, even Appellants agree that inhibition of gene expression via the claimed invention was known in the art. Therefore, the polyamides of Trauger, Swalley, and Parks which disclose polyamides comprising N-methylpyrrole, and N-methylimidazole amino acids would have been useful to inhibit both transcription factor binding and gene expression as recited in claims 25-26.

For the above reasons, it is believed that the rejections should be sustained.


Respectfully submitted,

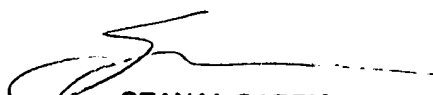

Janet L. Epps
Examiner
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